REMARKS

Claims 7 and 22 have been amended in this Amendment B. Specifically, claims 7 and 22 have been amended to remove the term "about." Claims 1-4, 6-10, and 15-25 will be pending upon entry of this Amendment B. Applicants respectfully request reconsideration and allowance of all pending claims.

1. Rejection of Claims 7 and 22 Under 35 U.S.C. §112

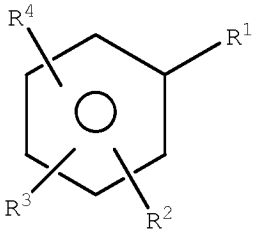
Claims 7 and 22 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully disagree, but have amended the claims to advance prosecution. Specifically, claims 7 and 22 have been amended to remove the term "about." Accordingly, Applicants submit that claims 7 and 22 comply with 35 U.S.C. § 112, second paragraph, and request that the rejection of these claims be withdrawn.

2. Rejection of Claims 1-4, 6-11, and 15-25 Under 35 U.S.C. §103(a)

Reconsideration is requested of the rejection of claims 1-4, 6-11, and 15-25 under 35 U.S.C. §103(a) as being unpatentable over Robbins et al. (J. Clin. Microbiol. 1987) and Lambert (J. Applied Microbiol.) in view of Syverson (U.S. 5,612,045) or Syverson in view of Robbins et al. and Lambert.

Claim 1 is directed to an exoprotein inhibitor for inhibiting the production of exoproteins from Gram positive

bacteria in and around a vagina. The exoprotein inhibitor comprises a **non-absorbent substrate for insertion into the vagina being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche.** The non-absorbent substrate has deposited thereon an effective amount of a first active ingredient and **an effective amount of a second active ingredient.** The first active ingredient has the general formula:



wherein R^1 is $-OR^6OH$; R^6 is a divalent saturated or unsaturated aliphatic hydrocarbyl moiety; R^2, R^3, and R^4 are independently selected from the group consisting of H, OH, COOH, and $-C(O)R^9$; R^9 is hydrogen or a monovalent saturated or unsaturated aliphatic hydrocarbyl moiety. The second active ingredient has the general formula:

$$R^{10}—O—R^{11}$$

wherein R^{10} is a straight or branched alkyl or straight or branched alkenyl having from 8 to about 18 carbon atoms and R^{11} is selected from the group consisting of an alcohol, a polyalkoxylated sulfate salt and a polyalkoxylated sulfosuccinate salt. Both the first active ingredient and second active ingredient are effective in inhibiting the production of exoprotein from Gram positive bacteria.

Robbins et al. disclose an analysis of the influence of 17 commercially available tampons on the production of toxic shock syndrome toxin 1 (TSST-1) by *S. aureus* using a tampon disk method. Specifically, a disk containing 10-ml of agar medium was overlaid with a Gelman GN-6 0.45-µm filter membrane and spread inoculated with 0.05 ml of an overnight still culture of *S. aureus* FRI-1169. In some samples, 10% blood was added to the agar medium. The test tampon was laid on the membrane and gently pressed down for uniform contact with the inoculated membrane. The disk was then sealed and incubated at 37°C for 19 hours. A plate count agar was used for enumeration of colonies in the tampon and membrane and a single gel diffusion tube method was used to determine the toxin content of the agar layer under the tampon and membrane. It was found that the amount of toxin produced increased with all tampons when blood was added to the agar medium, with an average of 42% over that without the addition of blood. Robbins et al. teach that one function of tampons may be to support the vaginal infection by supplying a fibrous surface for heavy colonization and to provide a sufficiently aerobic environment for toxin production.

Robbins et al. further disclose the effect of Aqualon, a surfactant, used alone or in combination with a deodorant in tampon manufacturing, on the growth and TSST-1 production by the *S. aureus*. It was found that while the Aqualon used alone on the tampon resulted in a decrease in CFU recovered from the tampon disk with a corresponding decrease in TSST-1 production associated with the disk, when blood was added to the agar, Aqualon showed little or **no effect on growth and TSST-1**

production by the *S. aureus* strain.[1] It was further shown, however, that when using the combined Aqualon and deodorant composition, there was a >50% decrease in the amount of TSST-1 recovered from both the agar layer and the tampon disk.[2]

Lambert discloses a method of examining the effect of inoculum size on the degree of inhibition observed with respect to inhibitor concentration. Specifically, the inoculum size dependencies of phenethyl alcohol, phenoxyethanol, *p*-chloro-*m*-cresol, trichloro-phenol, thymol, and dodecyltrimethylammonium bromide against *S. aureus* were analyzed. For all inhibitors examined, it was found that at lower inoculum levels, there was a greater biocidal effect, whereas at higher inoculum levels, there was a greater degree of quenching of the biocide, causing the inhibitor to act more as a simple (sublethal) inhibitor. As such, the method developed in Lambert may be used to quantify the effect in the region between reversible and irreversible damage, or sublethal injury to cell death. Furthermore, it was found in Lambert that phenethyl alcohol is a better inhibitor than phenoxyethanol against *S. aureus*.

Both Robbins et al. and Lambert fail to disclose the use of phenoxyethanol (or any compound having the structure of the first active ingredient) in combination with a second active ingredient **on a non-absorbent substrate being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche for insertion into the vagina** for inhibiting exoproteins from Gram positive bacteria as required in claim 1. Specifically, a

[1] Robbins, et al. on page 1448.

second active ingredient having the structure as required in claim 1 was **never even mentioned** in the cited references. In an attempt to find each and every element of claim 1 as required by the M.P.E.P. for a determination of *prima facie* obviousness, the Office cites the Syverson reference for combination with Robbins et al. and Lambert.

Syverson is merely directed to **absorbent** articles, such as catamenial tampons, which include an effective amount of an ether compound to substantially inhibit the production of exotoxins by Gram positive bacteria. In the Response to Arguments section of the final Office action, the Office states that Syverson teaches both absorbent and non-absorbent articles with *S. aureus* exoprotein inhibiting compounds. Specifically, the Office states, citing to Syverson at column 3, lines 50-60, that tampons may be absorbent or non-absorbent. With all due respect, Applicants assert that the Office is misconstruing the reference. In particular, although Syverson discloses at column 3, lines 56-58, that "the tampon may be made of various fiber blends including **both absorbent and nonabsorbent** fibers," (emphasis added) Syverson does not disclose that the tampon itself is nonabsorbent. In fact, the tampon as described in Syverson would not be effective for its intended use if the assembled tampon was non-absorbent. Accordingly, Syverson does not describe or suggest a non-absorbent substrate selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche. As such, Applicants submit that one skilled in the art would

[2] Id. at page 1449.

readily understand that a catamenial tampon is **not** a non-absorbent substrate, as required by Applicants' claim 1. Moreover, nowhere in Syverson is a first active ingredient as set forth in claim 1 even mentioned, much less that such a compound has antimicrobial properties or is effective in inhibiting the production of exoprotein from Gram positive bacteria when deposited on a non-absorbent substrate selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche.

In order for the Office to show a prima facie case of obviousness, M.P.E.P. §2142 requires a clear articulation of the reasons why the claimed invention would have been obvious. Specifically, the Supreme Court in KSR International Co. v. Teleflex Inc., 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007) noted that the burden lies initially with the Office to provide an explicit analysis supporting a rejection under 35 U.S.C. 103. "[R]ejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." The Court in KSR International further identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in Graham v. John Deere Co. (383 U.S. 1, 148 USPQ 459 (1966). Specifically, as previously required by the TSM (teaching, suggestion, motivation) approach to obviousness, one exemplary rationale indicated requires some teaching, suggestion, or motivation in the prior art reference that would

have led one of ordinary skill to modify the prior art reference to arrive at the claimed invention. Specifically, to reject a claim based on this rationale, the Office must articulate the following: (1) a finding that there was some teaching, suggestion, or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to arrive at each and every limitation of the claimed invention; (2) a finding that there was reasonable expectation of success; and (3) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. The Office has failed to meet its burden under number (1) above, as the cited references fail to show each and every limitation of Applicant's invention and there is no apparent reason for one skilled in the art to combine the reference teachings to arrive at each and every limitation. It simply would not have been obvious to one skilled in the art to arrive at Applicant's claimed combinations.

Specifically, as noted above, none of the cited references teach the use of a combination of a first active ingredient and a second active ingredient **on a non-absorbent substrate** for inhibiting exoprotein production. At best, Robbins et al. teach that the use of a combination of surfactant and deodorant during the manufacturing of a tampon may inhibit exoprotein production and growth of *S. aureus*. No where, however, is phenoxyethanol or the second active ingredient having the structure of claim 1 even mentioned. Furthermore, while Lambert does analyze

phenoxyethanol as one of six inhibitors that may inhibit exoprotein production, Lambert fails to teach or suggest the use of a second active ingredient with the pheoxyethanol to inhibit exoprotein production. In particular, no second active ingredient, either having the structure as required in claim 1 or otherwise, is even mentioned in Lambert. Furthermore, as noted above, Syverson fails to overcome these shortcomings as well.

Furthermore, the common sense of one ordinarily skilled in the art would not have provided a reason to combine the cited references to arrive at Applicants' exoprotein inhibitor comprising a first active ingredient and a second active ingredient having the structures as required in claim 1 deposited on a non-absorbent substrate. Applicants submit that even if one skilled in the art did select phenoxyethanol as the first active ingredient based on the teachings of Lambert, there is nothing in the cited references to motivate one to also include a second active ingredient, much less the specific second active ingredient of claim 1. Moreover, why would one skilled in the art be motivated to add the second active ingredient of claim 1 when Lambert teaches that phenoxyethanol already inhibits the exoprotein production? Based on the teachings of the cited references, there is simply no motivation to combine the cited references to arrive at Applicants' instant claim 1.

As none of the cited references teach or suggest using the first active ingredient and second active ingredient having the structures as set forth in claim 1 on a non-absorbent substrate

selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche for insertion into the vagina for inhibiting exoproteins from Gram positive bacteria, claim 1 is patentable over the combination of Robbins et al., Lambert, and Syverson.

Claims 2-4, 6-10, and 15-25 depend directly or indirectly on claim 1. As such, claims 2-4, 6-10, and 15-25 are patentable for the same reasons as claim 1 set forth above, as well as for the additional elements they require.

Conclusion

In view of the above, Applicants respectfully request favorable reconsideration and allowance of all pending claims. The Commissioner is hereby authorized to charge any fee deficiency in connection with this Amendment B and Response After RCE to Deposit Account Number 01-2384.

Respectfully Submitted,

/Christopher M. Goff/

Christopher M. Goff, Reg. No. 41,785
ARMSTRONG TEASDALE LLP
One Metropolitan Square, 26th Floor
St. Louis, Missouri 63102
314-621-5070

CMG/JMB/EMF
Via EFS